Released 04/06/99.

INSTRUCTIONS FOR COMPLETING THE NIH ANIMAL STUDY PROPOSAL (ASP) FORM

The Animal Welfare Act and the PHS Policy on Humane Care and Use of Laboratory Animals require review and approval of an Animal Study Proposal by the appropriate Animal Care and Use Committee (ACUC) prior to the conduct of <u>any</u> activity involving vertebrate animals.

GENERAL INSTRUCTIONS AND BACKGROUND:

The writing and review of animal study proposals serves several important functions including:

* Fulfilling statutory requirements,
* Alerting the investigator of possible limitations in the support services available (facilities, equipment, etc.),
* Alerting support staff (Division of Safety, Facility Veterinarians, etc.) of the type of support and space requirements needed.

The following instructions are provided to help the investigator develop an ASP which will meet all regulatory requirements and guidelines by which the proposal will be reviewed. If you are preparing an ASP using these instructions and are unclear as to what information is requested, additional information is available from your Institute, Center, or Division (ICD) Veterinarian's office, or the Chairperson of your ACUC.

A brief summary of the Animal Welfare Act regulations (9CFR) relating to protocol development and review are provided as Attachment 1. This attachment is provided to aid the investigator in understanding the regulatory requirements the ACUC is charged with ensuring each ASP meets before approval can be recommended. Additional references pertaining to ASP development and content include:

1. *Guide for the Care and Use of Laboratory Animals*, NIH Publication No. 85-23, revised 1985.
2. NIH Manual Issuance 3040-2, *"Care and Use of Animals in the Intramural Research Program"*, July 1, 1987.
3. Public Health Service *"Policy on Humane Care and Use of Laboratory Animals,"* revised September, 1986.
4. 1986 *"Report of the AVMA Panel on Euthanasia"*, JAVMA 188: 252-268, 1986.
5. *Biosafety in Microbiological and Biomedical Laboratories*, NIH Publication No. 88-8395, revised May, 1988.

REMEMBER:

* ASP forms must be legible. Only typed copies of the ASP are acceptable.

* Each section must be completed. Incomplete or illegible proposals will be returned before processing.

* All information in this proposal is considered privileged and confidential by the ACUC and the concurring authorities. However, approved proposals are subject to release to the public under the Freedom of Information Act. **DO NOT** include proprietary or classified information on the ASP form.

PART A: ADMINISTRATIVE DATA

The requested information identifies the Principal Investigator, the Project Title, and those authorized to perform animal activities under this proposal. The Principal Investigator must be a permanent staff member of the ICD to which the ASP will be submitted. Purchase requests for animals may only be initiated by individuals listed on the proposal. Indicate if this is an initial ASP, a renewal, or a modification. If this is a renewal or modification, cite the original proposal number. **Any significant modification to proposals must be reviewed and approved by the ACUC before that change is implemented.**

PART B: ANIMAL REQUIREMENTS

This section requests identification of the species and the strain/stock designation of the animal. Animals obtained from non-approved sources may require completion of Form NIH 2369-1, Application for Permit to Introduce Rodents and Rodent Products. Indicate the proposed location for animal holding (building and room). If the animals will be housed in more than one location, identify each area where animals will be held for greater than 12 hours. Estimate the number of animals to be used each year of the approval period and the total number of animals to be used. (ASPs may be approved for a maximum of three years.) Estimate the maximum number of animals to be housed at any one time. Note that a request to increase the number of animals can be made at any time by submitting a written statement that includes a justification for additional animals to the ACUC. If surgically altered animals, e.g., adrenalectomized, splenectomized, etc., or other animals requiring special care are needed in the study, your requirements should be described in part M, "Special Concerns or Requirements of the Study".

PART C: TRANSPORTATION

Transportation of animals must conform with the "NIH Animal Transportation Guidelines", and provide for the security and safety of the animals and humans involved. If transportation is to occur between buildings, VRP transportation is recommended, and may be required. Many buildings have specific transportation policies specifying which elevators, hallways, etc., may be used when transporting animals. If you are uncertain of the policies applicable to your study's location(s), additional information is available from your Institute Veterinarian's office, VRP (phone 496-3347), or the NIH Office of Animal Care and Use, NCRR (496- 5424).

Assurances must be provided that animals exposed to biologic hazards or containing radioactive material will be properly contained, and minimize occupational exposures and environmental contamination while being moved from one location to another. If a vehicle is used, it must be properly designed and designated for the transportation of animals.

PART D AND E: STUDY OBJECTIVES and RATIONALE FOR USE OF ANIMALS

The objectives and significance of the study should be written in terms that will clearly demonstrate to lay audiences the importance of this work. The rationale and requirement to use animals should be described in non-technical terms. The Animal Welfare Act requires the ACUC "ensure that the type and number of animals proposed are appropriate and necessary" to accomplish the goals of the project. This section should provide the rationale for:

a. <u>The use of animals</u>, e.g., why cell culture or computer simulations cannot be used instead of animals.

b. The appropriateness of the species being used, e.g., why a lower order mammal, invertebrate, etc., can't be used.

c. The number of animals to be used, e.g., the number of animals per experimental group times the number of groups in each experiment times the number of experimental replications; or the amount of tissue needed for the study divided by the amount of tissue to be obtained from each animal; or a historical or projected number required per assay, month, etc., times the number of assays, months, etc., expected during the study. (PHS policy specifies that studies use the minimum number of animals required to obtain valid results.)

PART F: DESCRIPTION OF EXPERIMENTAL DESIGN AND ANIMAL PROCEDURES

This section is intended to give an overview of the study, and clarify how the experimental procedures will accomplish the study objectives. Details of individual animal procedures should also be provided. Flow charts, time lines, etc., may be helpful to demonstrate how different parts of the study are related.

The Animal Welfare Act regulations require that animal study proposals contain a "complete description of the proposed use of the animals", and charges the ACUC with reviewing the ASP to ensure it meets 11 major specified requirements (see attachment 1) before the committee can recommend approval. If the ACUC cannot visualize each of the procedures being performed on the animals, it cannot properly discharge its responsibility. Details of each procedure which may impact on the pain or stress potential of that procedure should be specified. The following list of details to be specified for commonly performed procedures can be used as a guide of the level of detail required.

* Injections or inoculations: substance, dose, volume, sites, route, and schedule
* Blood/fluid collection: volume, frequency, withdrawal sites, and method
* Radiation: dose/activity and schedule
* Restraint: type (chair, sling, harness, etc.), length of time restrained, any conditioning/training required
* Animal identification method: type (ear punch, ear notch, collar, cage card, tattoo, etc.)
* Food restriction: degree of restriction (% baseline body weight, complete, etc.), period of time restricted, method and frequency of monitoring

If any of the procedures are likely to create significant symptomatology or death, a description of the experimental endpoints should be included (e.g., tumor size, % body weight gain or loss, inability to eat or drink, behavioral abnormalities, clinical symptomatology, signs of toxicity, etc.). The action to be taken once the end point has been reached should also be included (e.g., animal euthanized, removed from study, veterinary consultation requested, etc.).

PART G: SURVIVAL SURGERY

Survival surgery is defined as a surgical procedure from which the animal is allowed to recover from anesthesia. Non-survival surgery, in contrast, is a surgical procedure in which the animal is euthanized prior to recovery from anesthesia. A major operative procedure is one that penetrates and exposes a body cavity, or any procedure which produces permanent impairment of physical or physiological function.

1. Identify the surgical procedure(s) to be performed.

2. Any surgery to be performed should be described, including the use of aseptic technique, and the dose and route of administration of anesthetic. A brief description of the parameters used to monitor level of anesthesia during surgery, e.g., vital signs, muscle tone, etc., should be included.

If animals are to be paralyzed with chemical agents under anesthesia, anesthetic monitoring is critical. Please include parameters used to determine when more anesthetic is to be given. A reference indicating these are accepted parameters should be included.

3. Regulations charge the ACUC with ensuring individuals performing animal procedures are qualified through training and experience. Provide the names of individuals performing animal surgery, and their qualifications to perform the specific procedures listed.

4. Survival surgery on rodents must be performed using aseptic technique in a suitably prepared area. Aseptic technique and specialized/dedicated surgical facilities are required for survival surgery proposed in rabbits and other higher species such as cats, dogs, and nonhuman primates. Specify the building and room number where any survival surgeries will be performed.

5. In the description of recovery/post surgical care, include any needed supportive therapy (external heat pads, IV fluid support, etc.); any surgical site or catheter care procedures; specialized diets, antibiotics, analgesics, etc.; and the approximate length of time the animal will be maintained between surgery and the end of its use in the project. Also include observations necessary to evaluate animal's recovery and continued good health, e.g., daily observation of: surgical site for proper healing, proper appetite, weight maintenance, etc. Method(s) of handling potential postoperative complications should be briefly described, e.g. veterinary consultation and assistance will be obtained.

Unless veterinary support has been arranged, at least one of the individuals responsible for post-operative care should be available to provide care, if needed, after hours and on weekends and holidays.

6-7. The Animal Welfare Act regulations specify, "No animal will be used in more than one major operative procedure from which it is allowed to recover, unless: (A) Justified for scientific reasons by the principal investigator, in writing;...". Economic cost of additional animals is not an acceptable justification for performing multiple major survival surgeries on the same animal. Many "surgically modified" animals (e.g., adrenalectomized, splenectomized, etc.), have received a major survival surgery prior to being placed on the study, and cannot receive an additional major survival surgery during the study unless justified as scientifically necessary to accomplish the goals of the study.

PART H: PAIN or DISTRESS CATEGORY

The Animal Welfare Act regulations require each research facility to report annually the numbers of animals used in research. The report must list the numbers of animals which were used in studies involving:

1. "no pain or distress" (listed in Column C),

2. "pain or distress where appropriate anesthetic, analgesic, or tranquilizing drugs were administered" (listed in Column D), and

3. "pain or distress without the administration of appropriate anesthetic, analgesic, or tranquilizing drugs (listed in Column E).

While it is recognized that it will often be impossible to provide the precise number of animals which will be used in each category before the study begins, an estimate is requested.

Any project involving a Column E listing requires the form "Explanation for Column E Listings" be completed and attached to the ASP at the time of submission. **This form will be forwarded to the USDA with the annual report, and is available to the PUBLIC under the Freedom of information Act.**

See Attachment 1 of the ASP form for additional definitions and guidelines for classifying the types of procedures to be performed.

PART I: ANESTHESIA, ANALGESIA, TRANQUILIZATION

Type and dose of anesthetic, analgesic, and tranquilizer or sedative must be appropriate for both the species being used and the type pain or distress being prevented/relieved. Doses and routes of administration should be clearly appropriate and effective, i.e., commonly accepted or published doses, or experience with that agent and dose described which demonstrates its effectiveness.

The schedule or indications for administration should be provided, e.g. every 12 hours, as needed, etc. If agents are to be given "as needed", a brief description of the indications for its administration should be provided, e.g., "at the first indication of discomfort as evidenced by lethargy, anorexia, hunched posture, eye squinting, or vocalization."

PART J: METHOD OF EUTHANASIA OR DISPOSITION OF ANIMALS AT END OF STUDY

The Animal Welfare Act regulations specify that each ASP contain a description of any euthanasia methods to be used. PHS policy specifies that methods which are not consistent with the recommendations of the AVMA Panel on Euthanasia must be justified scientifically, in writing.

Animal carcasses which have not been contaminated with hazardous agents (chemical, biological, or radioactive) are to be disposed as Medical Pathological Waste in accordance with NIH guidelines. Radiation Safety Branch (phone: 496-5774) should be consulted on proper disposal methods for carcasses contaminated with radioactive material. Division of Safety personnel (phone: 496-2346) should be consulted on proper disposal methods for carcasses contaminated with other hazardous agents.

If animals are not going to be euthanized as a part of the study, or at the conclusion of the study, specify the disposition of the live animals, e.g., "Animals will be returned to the veterinary section for reissue at the conclusion of the study."

PART K: HAZARDOUS AGENTS

This section must be completed if hazardous agents will be used in animals. Use of hazardous agents requires the concurrence of the safety representative in part O. For each type agent used, specify the information listed below:

> **Radioisotopes:** Identify radioactive isotopes used and their activity. Depending on the activity, a Radiation Safety Protocol may be necessary. Health Physicist signature required.
>
> **Biological Agents:** List viruses, bacteria, and any blood or body fluids potentially infectious to humans. A Human Pathogen Registration Document must be filed with the Occupational Safety and Health Branch (OSHB) for these biologicals. Identify the registration document number (RD#). Safety Specialist signature required.

Hazardous Chemical or Drugs: List any hazardous chemicals or drugs, e.g., carcinogens, mutagens, all inhalation anesthetics, toxins, etc. Safety Specialist signature required.

Recombinant DNA: Identify any nonexempt Recombinant DNA made in the course of this study. If study involves developing transgenic animals identify them in this area. A recombinant DNA registration document must be filed with the NIH Institutional Biosafety Committee (IBC) for all nonexempt Recombinant DNA experiments. Identify the RD#. Safety Specialist signature required.

For definitions of Biosafety Level see reference 5 listed on page one of these instructions.

Describe the practices and procedures required for the safe handling and disposal of contaminated animals and material associated with this study. Also describe methods for storage/removal of radioactive waste, and monitoring of the area.

After review of your ASP, the safety representative may specify/clarify any additional safety precautions which must be incorporated in the ASP.

PART L: BIOLOGICAL MATERIAL/ANIMAL PRODUCTS

Principal Investigators are responsible for ensuring that the animals and biologic materials used in their study do not present a risk to the other animals housed in an animal facility.

Biological material and animal products (cell lines, tissues, and tumors) have been incriminated repeatedly as vehicles for the introduction of contagious organisms, e.g., ectromelia, LCM, and mouse hepatitis virus. NIH Manual 3043-1 requires NCRR/VRP approval before the introduction of any rodent, rodent product, or biologicals, that may harbor agents of animal diseases considered dangerous to the programs of the NIH. NIH Form 2369-1, Application for Permit to Introduce Rodents and Rodent Products, must be submitted through the Institute Veterinarian for approval before animals or animal products from unapproved sources are introduced into any NIH or ICD facility. If it is not certain that the biological materials/animal products to be used have been produced and maintained in a manner which excludes/eliminates any potential pathogens they may be required to be Mouse Antibody Production (MAP), Rat Antibody Production (RAP), or Hamster Antibody Production (HAP) tested before being transported to NIH facilities.

PART M: SPECIAL CONCERNS OR REQUIREMENTS OF THE STUDY

List any requirements that animal facility personnel need to be aware of to ensure the proper care of the animals on this study, or to properly support this study. Such requirements include any specialized housing, lighting, feed, or water; a need for other than routine veterinary care; use and storage of specialized equipment; or special after hours or weekend/holiday requirements. If holding of animals in laboratories for more than 12 hours will be necessary, it should be described.

If surgically altered animals are needed for this study, i.e., adrenalectomized, splenectomized, etc., their surgical modification, source, and any special care requirements should be described.

PART N: PRINCIPAL INVESTIGATOR CERTIFICATIONS

Each certification listed is designed to meet specific requirements of the Animal Welfare Act regulations, the "PHS Policy", or NIH policy. Information and assistance in accomplishing tasks required by this section, e.g., training requirements, enrollment in the NIH Animal Exposure Surveillance Program, etc., is available through the ICD Veterinarian's office.

Item 5 reflects the Animal Welfare Act regulations requirement that, "The principal investigator has considered alternatives to PROCEDURES that may cause more than momentary or slight pain or distress to the animals, and has provided a written narrative description of the methods and sources, e.g., the Animal Welfare Information Center, used to determine that alternatives were not available...". Examples of methods and sources used may include, but are not limited to, the following:

Databases searched, and the key words used in the searches. Examples include:

AGRICOLA	MEDLINE
AIDSLINE	TOXLINE
AVLINE	TOXLIT
CANCERLIT	TOXNET

Pertinent references, bibliographies, or other publications.

Information services utilized. Examples include:

Animal Welfare Information Center, phone: (301) 504-6212.
Primate Information Center, phone: (206) 543-4376.
Primate Information Clearinghouse, phone: (206) 543-5178.
Scientists Center for Animal Welfare, phone: (301) 654-6390.

Consultation with individuals having expertise in the field of investigation.

Comments should only be included in item 5 if the study involves PROCEDURES which may cause more than momentary or slight pain or distress to the animals. This section SHOULD NOT address why animals are necessary in the study (that information should be presented in part E).

PART O: CONCURRENCES

Before an ASP is submitted for ACUC review, it must be reviewed and approved on the basis of its scientific merit. The scientific merit review is to be performed by the investigator's Laboratory Chief. If the Principal Investigator is a Laboratory Chief, the proposal must be approved by the next higher level of scientific review authority, e.g., Scientific Director.

If hazardous agents are to be used in animals during the study, the ICD's Safety and/or Radiation Safety representative's approval is required before submission of the proposal.

The facility manager/veterinarian's certification that adequate resources are available to support the study is required to assure the ACUC that appropriate animal care will be available to the animals during the study. The facility manager/veterinarian's signature DOES NOT guarantee that space will be available at the time the investigator wishes to start the study. It only signifies that appropriate facilities, equipment, personnel, etc., are available within that facility to properly and safely support the study. Some animal facilities may require additional information from the investigator prior to housing animals for a particular study. A facility manager/veterinarian's signature should be obtained for each of the animal facilities where animals will be housed during the study.
Animal Welfare Act regulations require painful/distressful procedures "involve, in their planning, consultation with the attending veterinarian..." The attending veterinarian's initial review is also used to ensure significant animal welfare issues are addressed before submission to the ACUC.

PART P: FINAL APPROVAL

Self-explanatory.

Attachments:

1. Animal Welfare Act regulations (9 CFR): selected text summary.

Attachment 1

ACUC Review of Animal Study Proposals:

Regulatory Requirements

(9 CFR, Subchapter A, "Animal Welfare")

1. In order to approve proposed activities or proposed significant changes, the committee must review "those components of the activities related to the care and use of animals" and determine they are in accordance with 9 CFR Subchapter A, and meet "the following requirements":

(i) The study is designed to avoid or minimize discomfort, distress, and pain to the animals.

(ii) The principal investigator (PI) has considered alternatives to procedures that may cause pain or distress, and provided a written narrative description of the methods and sources (e.g. Animal Welfare Information Center), used to determine that alternatives are not available.

(iii) The PI has provided a written assurance the activities do not unnecessarily duplicate previous experiments.

(iv) Painful/distressful procedures will:

(A) be performed with appropriate sedatives, analgesics, or anesthetics (SAA). Withholding SAA must be justified for scientific reasons, and continue for only the necessary period of time.

(B) Involve consultation with attending veterinarian in their planning.

(C) NOT include use of paralytics without anesthesia.

(v) Animals which would experience chronic unrelieved pain or distress will be euthanized during or after the procedure.

(vi) Animals will be housed in accordance with 9 CFR.

(vii) Medical care will be available and provided by a veterinarian.

(viii) Personnel conducting animal procedures are appropriately qualified and trained in those procedures.

(ix) All surgical procedures will include appropriate pre-and post-operative care. All survival surgery will be performed aseptically using surgical gloves, masks, sterile instruments, and aseptic technique. Major operative procedures on non-rodents will be conducted only in dedicated facilities.

(x) No animal will be used in multiple major survival surgery, unless:

(A) Justified for scientific reasons,
(B) Required for veterinary care,
(C) Special circumstances determined by Administrator, USDA.

(xi) Methods of euthanasia meet definition in part 1, 9 CFR, unless deviation justified in writing. (PHS policy specifies procedures recommended by AVMA Panel.)

Proposals and significant changes must contain:

(1) The species and approximate number of animals to be used;

(2) The rationale for using animals, appropriateness of the species AND numbers of animals to be used; (PHS Policy specifies: species, quality, and minimum number required to obtain valid results.)

(3) A complete description of the proposed use of the animals;

(4) A description of procedures, including use of SAA, designed to assure that discomfort and pain will be limited to that which is unavoidable for the conduct of scientifically valuable research.

(5) Description of any euthanasia methods to be used.

ATTACHMENT I

Guidelines for Pain/Distress Classification
(For guidance only in categorizing animal use in Section H.)

Definitions:

Pain is awareness of acute or chronic discomfort occurring in varying degrees of severity resulting from injury, disease, or emotional distress and evidenced by biological or behavioral changes or both.

Acute Pain results from a traumatic, surgical, or infectious event that is abrupt in onset, relatively short in duration, and generally alleviated by analgesics. Associated distress may be responsive to tranquilizers.

Chronic Pain results from a long standing physical disorder or emotional distress that is usually slow in onset, has a long duration, and is generally not totally alleviated by analgesics, but frequently responds to tranquilizers combined with environmental manipulation and behavioral conditioning.

Distress is undesirable physical or mental stress resulting from pain, anxiety, or fear. Its acute form may be relieved by tranquilizers, while sustained distress requires environmental change and behavioral conditioning, and does not respond to drug therapy.

Column C - Minimal, transient, or no pain or distress
These procedures are considered to produce minimal, transient, or no pain or distress when performed by competent individuals using recognized methods.

1. Administration of:
   a. Anesthetics, analgesics, and tranquilizers
   b. Fluid and electrolyte therapy
   c. Immunizations
   d. Oral medications
2. Non-chronic catheterization
3. Blood collection (except intracardiac, and periorbital in some species, see below)
4. Gastric gavage
5. Certain procedures performed in the normal practice of veterinary medicine and those involving the diagnosis and treatment of disease (e.g., injections, palpations, skin scraping, radiography).
6. Euthanasia as performed in accordance with recommendations of the AVMA Panel on Euthanasia.
7. Intracerebral inoculations in neonatal rodents. In many neonatal rodents intracerebral inoculations can be performed by trained personnel prior to cranial ossification, producing only transient pain or distress. If the result of any of the above procedures is painful or distressful the procedure should be listed under Category 2 or Category 3 below.

Column D - Pain or distress relieved by appropriate measures

Examples of procedures that may produce pain or distress, but which are performed using appropriate and adequate anesthetics, analgesics, or tranquilizers and followed with appropriate measures to alleviate pain or distress are as follows:

1. All surgery, including biopsy, gonadectomy, and neurophysiological manipulations or preparations such as implantation of electrodes and recording devices, and alterations to nerve or muscle fibers.
2. Burning, freezing, and branding.
3. Fracturing bones.
4. Electrical shocks including shock reinforcement, using voltage which is accepted as generally causing pain in humans.
5. Use of any agent that induces excessive inflammation or necrosis.
6. Drug or radiation toxicity testing, including LD_{50} determinations, producing pain and distress.
7. Chair or stock restraint of unadapted animals, or of any animal for more than 12 hours.
8. Skin or corneal corrosivity testing, including Draize testing.
9. Intracardiac blood collection.
10. Periorbital collection of blood from any species except mice and hamsters. Note: Periorbital collection from unanesthetized animals that do not possess a true orbital sinus, as do mice and hamsters, is discouraged.

Column E - Unrelieved pain or distress

Procedures, including those listed above for Category 2, which are performed without appropriate and adequate anesthesia, analgesia, or tranquilizers or which are not followed with appropriate measures to alleviate pain or distress, or which are not amenable to relief by therapeutic measures, must be listed in Category 3.

ATTACHMENT II

GUIDANCE FOR COMPLETION OF PART N. "PRINCIPAL INVESTIGATOR CERTIFICATION"

1. This is a mandatory requirement of NIH Policy: NIH Manual Issuance 3040-2, "Care and Use of Animals in the Intramural Research Program"

2. This certification is a legal requirement of the U.S. Animal Welfare Act

3. A written narrative description of the methods and sources used to determine that alternatives to painful or distressful procedures are not available, whether or not the pain or distress is alleviated, is also required by the U.S. Animal Welfare Act. Examples of this may include, but are not limited to the following:

   - Databases searched and the key words used in the searches. Examples include:

AGRICOLA	MEDLINE
AIDSLINE	TOXLINE
AVLINE	TOXLIT
CANCERLIT	TOXNET

   - Pertinent references, bibliographies, or other publications.

   - Information services utilized. Examples include:

     Animal Welfare Information Center, USDA
     Primate Information Center
     Primate Information Clearinghouse
     Scientists Center for Animal Welfare

   - Consultation with individuals having expertise in the field of investigation.

NATIONAL INSTITUTES OF HEALTH
ANIMAL STUDY PROPOSAL

Leave Blank

Proposal # _____

Approval Date _____

Expiration Date _____

Please Type

A. ADMINISTRATIVE DATA:

Institute, Center, or Division	
Principal Investigator	
Building/Room	
Telephone	
Fax	
Division, Laboratory, or Branch	
Project Title	

Initial Submission [ ] Renewal [ ] or Modification [ ] of Proposal Number _____

List the names of all individuals authorized to conduct procedures involving animals under this proposal and identify key personnel (i.e., Co-investigator(s)):

B. ANIMAL REQUIREMENTS:

Species	
Stock/Strain	
Age/Weight/Size	
Sex	
Source(s)	
Animal Holding Location(s)	
Animal Procedure Location(s)	

Number of Animals To Be Used	Year 1	Year 2	Year 3	TOTAL

C. TRANSPORTATION: Transportation of animals must conform to all NIH and Facility guidelines/policies. If animals will be transported between facilities, describe the methods and containment to be utilized. If animals will be transported within the Clinical Center, also include the route and elevator to be utilized.

D. STUDY OBJECTIVES: Briefly explain in non-technical terms the aim of the study and why the study is important.

E. RATIONALE FOR USE OF ANIMALS: I) Explain your rationale for animal use. 2) Justify the appropriateness of the species selected. 3) Justify the number of animals to be used.

F. DESCRIPTION OF EXPERIMENTAL DESIGN AND ANIMAL PROCEDURES: Briefly explain the experimental design and specify all animal procedures performed. This description should allow the ACUC to understand the experimental course of an animal from its entry into the experiment to the endpoint of the study. Specifically address the following:

- Injections or Inoculations (substances, e.g., infectious agents, adjuvants, etc.; dose, sites, volume, route, and schedules).

- Blood withdrawals (volume, frequency, withdrawal sites, and methodology).

- Non-survival surgical procedures (Provide details of survival surgical procedures in Section G.)

- Radiation (dosage and schedule)

- Methods of restraint (e.g., restraint chairs, collars, vests, harnesses, slings, etc.)

- Animal identification methods (e.g., ear tags, tattoos, collar, cage card, etc.)

- Other procedures (e.g., survival studies, tail biopsies, etc.).

- Resultant effects, if any, the animals are expected to experience (e.g., pain or discomfort, ascites production, etc.)

- Experimental endpoint criteria (i.e., tumor size, percentage body weight gain or loss, inability to eat or drink, behavioral abnormalities, clinical symptomatology, or signs of toxicity) must be specified when the administration of cells, biologics, infectious agents, radiation or toxic chemicals are expected to cause significant symptomatology or are potentially lethal.

G. SURVIVAL SURGERY - If proposed, complete the following:

1. Describe the surgical procedure(s) to be performed. Include the aseptic methods to be utilized. (Use additional sheets if necessary):

2. Who will perform surgery and what are their qualifications and/or experience?

3. Where will surgery be performed? Building and Room? _____ - _____

4. Describe post-operative care required and identify the responsible individual:

5. Has major survival surgery been performed on any animal prior to being placed on this study? Y/N [____]. If yes, please explain:

6. Will more than one major survival surgery be performed on an animal while on this study? Y/N [____]. If yes, please explain:

H. PAIN OR DISTRESS CATEGORY - (See instructions for definitions and guidelines.) Check the appropriate category(ies) and indicate the approximate number of animals in each. Sum(s) should equal total from Section B.

	Number of animals to be used each year		
	YEAR 1	YEAR 2	YEAR 3
USDA Column C - Minimal, Transient, or No Pain or Distress			
USDA Column D - Pain or Distress Relieved By Appropriate Measures			
USDA Column E - Unrelieved Pain or Distress***			

***IF ANIMALS ARE INDICATED IN COLUMN E, A SCIENTIFIC JUSTIFICATION IS REQUIRED TO EXPLAIN WHY THE USE OF ANESTHETICS, ANALGESICS, SEDATIVES OR TRANQUILIZERS DURING AND/OR FOLLOWING PAINFUL OR DISTRESSFUL PROCEDURES IS CONTRAINDICATED. PLEASE COMPLETE THE EXPLANATION FOR COLUMN E LISTINGS FORM AT THE END OF THIS DOCUMENT. THIS FORM WILL ACCOMPANY THE NIH ANNUAL REPORT TO THE USDA AND IS AVAILABLE UNDER THE FREEDOM OF INFORMATION ACT.

I. ANESTHESIA, ANALGESIA, TRANQUILIZATION - For animals indicated in Section H, column D, specify the anesthetics, analgesics, sedatives or tranquilizers that are to be used. Include the name of the agent(s), the dosage, route and frequency of administration.

J. METHOD OF EUTHANASIA OR DISPOSITION OF ANIMALS AT END OF STUDY: Indicate the proposed method, and if a chemical agent is used, specify the dosage and route of administration. Indicate the method of carcass disposal, if not as Medical Pathological Waste (MPW).

K. HAZARDOUS AGENTS: Use of hazardous agents requires the approval of an ICD safety specialist. Registration Documents are required to be attached for the use of recombinant DNA or potential human pathogens.

	Yes	No	List agents and registration document number (if applicable)
Radioisotopes			
Biological Agents			
Hazardous Chemicals or Drugs			
Recombinant DNA			
Study conducted at Biosafety Level			

Describe the practices and procedures required for the safe handling and disposal of contaminated animals and material associated with this study. Also describe methods for removal of radioactive waste and, if applicable, the monitoring of radioactivity.

Additional safety considerations:

L. BIOLOGICAL MATERIAL/ANIMAL PRODUCTS (e.g., cell lines, antiserum, etc.):

1. Specify Material

2. Source

	Yes	No
Material Sterile or Attenuated		
3. If derived from rodents, has the material been MAP/RAP/HAP Tested? If yes, attach copy of results		

4. I certify that the MAP/RAP/HAP tested materials to be used have not been passed through rodent species outside of the animal facility in question and/or the material is derived from the original MAP tested sample. To the best of my knowledge the material remains uncontaminated with rodent pathogens.

_____ Initials of Principal Investigator.

M. SPECIAL CONCERNS OR REQUIREMENTS OF THE STUDY - List any special housing, equipment, animal care (i.e., special caging, water, feed, or waste disposal, etc.).

N. PRINCIPAL INVESTIGATOR CERTIFICATIONS - (See instructions for further guidance.):

1. I certify that I have attended an approved NIH investigator training course.

Year of Course Attendance		Location	

2. I certify that I have determined that the research proposed herein is not unnecessarily duplicative of previously reported research.

3. I certify that all individuals working on this proposal are participating in the NIH Animal Exposure Surveillance Program.

4. I certify that the individuals listed in Section A are authorized to conduct procedures involving animals under this proposal have received training in the biology, handling, and care of this species; aseptic surgical methods and techniques (if necessary); the concept, availability, and use of research or testing methods that limit the use of animals or minimize distress; the proper use of anesthetics, analgesics, and tranquilizers (if necessary); procedures for reporting animal welfare concerns.

5. FOR ALL COLUMN D AND E PROPOSALS (see Section H): I certify that I have received the pertinent scientific literature and the sources and or databases as noted below and have found no valid alternative to my procedures described herein which may cause more than momentary pain or distress. The methods and sources used in my search included the following:

6. I will inform the ACUC of any proposed significant changes in this study.

Principal Investigator: Signature _____ Date _____

O. CONCURRENCES: Proposal NUMBER _____

Laboratory/Branch Chief certification of review and approval on the basis of scientific merit. Scientific Director's signature required for proposals submitted by a laboratory or branch chief.

Name _____ Signature _____ Date _____

Safety Representative certification of review and approval. (Required of all studies utilizing hazardous agents.)

Name _____ Signature _____ Date _____

Facility Manager/Veterinarian certification of resource availability in the indicated facility to support the proposed study.

Facility _____ Name _____ Signature _____ Date _____

Facility _____ Name _____ Signature _____ Date _____

Facility _____ Name _____ Signature _____ Date _____

Facility _____ Name _____ Signature _____ Date _____

COMMENTS:

Attending Veterinarian certification of review.

Name _____ Signature _____ Date _____

P. FINAL APPROVAL:

Certification of review and approval by the _____ Animal Care and Use Committee Chairperson.

Chairperson _____ Signature _____ Date _____

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
National Institutes of Health

Memorandum

Date :

From :

Subject : Addendum to Protocol #

To : Animal Care and Use Committee

Project Title:

Describe changes to the above protocol:

CONCURRING AUTHORITIES

Laboratory Chief _____ Signature _____

Attending Veterinarian _____ Signature _____

Chairperson _____ Signature _____

Date Approved _____